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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,694	02/12/2002	C. Ronald Kahn	10276-017002 / JDP-031 Co	1080

26161 7590 10/06/2004

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,694	KAHN ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-37* is/are pending in the application.

4a) Of the above claim(s) *4-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 17-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 7-26-04.

Claims 2-37 are pending in the instant application.

Election/Restrictions

Applicant's election without traverse of Group I, claims 2,3 and 17-37 in the reply filed on 7-26-04 is acknowledged.

Applicant's election of Group I, claims 2, 3, 17-37 in the reply filed on 7-26-04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 4-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7-26-04.

The restriction requirement mailed 5-21-04 did not state that claim 2 was being treated as a linking claim. In order to provide Applicant with the opportunity to have claim 2 examined as part of the elected invention, claim 1 has been examined as a linking claim in the Office action set forth below.

Claim 2 link(s) inventions drawn to methods of modulating an activity of Rad in a cell. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 2. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and

any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Specification

The attempt to incorporate subject matter into this application by reference to the various citations listed on page 13, line 6-page 14, line 3 of the instant specification is improper because the polypeptide sequences (e.g. of nm23 or Rad) intended to be incorporated are not specifically described in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 17-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to compositions and methods for modulating an activity of Rad in a cell in vitro or in vivo comprising modulating the level of nm23 polypeptide, including comprising the administration of an nm23 polypeptide, a fragment of nm23 polypeptide or a homolog of nm23 polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide to the cell.

The specification, claims and art do not indicate what distinguishing attributes are concisely shared by members of the genus comprising an nm23, nm23H1 or nm23H2 polypeptide, a fragment of nm23 polypeptide, or a homolog of nm23 polypeptide that, when administered to a cell, modulates the activity of Rad in that cell. No sequences were provided in the instant disclosure for any members of this broad genus comprising nm23, nm23H1 or nm23H2 polypeptides, or fragments or homologs of nm23 polypeptide. The specification does not place any limit on the number of amino acid substitutions, deletions, insertions or additions that may be made to the members of this broad genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number structural differences between genus members is permitted. Concise structural features that could distinguish compounds in the genus from others are missing from the disclosure and the art. No common structural features or attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description

because specific, not general guidance is what is needed. (See the NCBI search report that lists numerous forms of nm23, nm23H1 and nm23H2 polypeptides, obtained from an array of species, e.g. including various isoforms from fly, chicken, rat, mouse and human). Since the disclosure fails to describe the common attributes or characteristics concisely identifying members of the proposed genus, and because the genus is highly variant, the description provided is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus claimed. Thus, Applicant was not in possession of the claimed genus.

Claims 2, 3, 17-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modulating Rad activity in vitro using nm23 polypeptide of undisclosed sequence, does not reasonably provide enablement for methods of modulating Rad activity in vivo comprising the administration of an nm23 polypeptide, a fragment of nm23 polypeptide or a homolog of nm23 polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide to the cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to methods of modulating an activity of Rad in a cell in vitro or in vivo comprising modulating the level of nm23 polypeptide, comprising the administration of an nm23 polypeptide, a fragment of nm23 polypeptide or a homolog of

nm23 polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide to the cell.

The state of the prior art and the predictability or unpredictability of the art. The following references are cited herein to illustrate that the delivery of polypeptides to a target cell in vitro or in vivo is energy dependent and requires the presence of specific proteins that serve as receptors and or channels. Derossi et al teach the ability of antennapedia homeodomain to translocate through biological membranes, but this ability is highly sequence dependent, and illustrates that delivery of polypeptides to target cells in vitro or in vivo is a rate limiting step for cell targeting and entry for most polypeptides (see D. Derossi et al. J. Biol. Chem. 269(14): 10,444-10,450, especially the abstract on p. 10,444, last paragraph of the introduction on p. 10,444; first full paragraph on p. 10,450: "Other polypeptides that cross biological membranes are those destined, after synthesis, to specific intracellular compartments such as the endoplasmic reticulum or the mitochondria... Passage through these intracellular membranes is energy-dependent and requires the presence of specific proteins that serve as receptors and/or channels. However, even in this rather well studied system, the actual mechanism of importation is not yet completely understood." For specific requirements of other, specialized polypeptides involved in cellular membrane penetration, see M. Pooga et al. FASEB J. 12: 67-77 for a discussion of the remarkable properties of transportan; see also G. Elliott et al, Cell 88 : 223-233 for the distinguishing features of Herpes virus structural protein and its role in intercellular trafficking)

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided adequate guidance in the specification toward a method of modulating Rad activity in a cell in vivo comprising the administration of an nm23 polypeptide, a fragment of nm23 polypeptide or a homolog of nm23 polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide to the cell. The specification very generally discusses co-precipitation experiments indicating a relationship between Rad and nm23 and in promoting GTP hydrolysis (see page 11, line 13-page 12, line 4 of the instant specification). No polypeptide sequences have been disclosed for nm23, nm23H1 or nm23H2 polypeptides. One skilled in the art would not accept on its face the examples given in the specification of the in vitro observations of biochemical links between nm23 and Rad as being correlative or representative of the successful modulation of Rad by nm 23 in an organism, in view of the lack of guidance in the specification and known unpredictability associated with the successful targeting and delivery of polypeptides to target cells harboring Rad in an organism, and further whereby modulation of Rad occurs in an organism comprising the administration of an nm23 polypeptide, a fragment of nm23 polypeptide or a homolog of nm23 polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide to the cell.

The breadth of the claims and the quantity of experimentation required. The claims are drawn to methods of modulating an activity of Rad in a cell in vitro or in vivo comprising modulating the level of nm23 polypeptide, comprising the administration of an nm23 polypeptide, a fragment of nm23 polypeptide or a homolog of nm23

polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide to the cell. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of accessible target sites, modes of delivery and formulations to target appropriate cells and /or tissues harboring Rad, whereby Rad activity is modulated following the administration by any route of an nm23 polypeptide, a fragment of nm23 polypeptide or a homolog of nm23 polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide to the cell in an organism. Since the specification fails to provide any particular guidance for inhibiting the modulation of Rad activity following administration of an nm23 polypeptide of disclosed sequence, or any fragment of nm23 polypeptide or any homolog of nm23 polypeptide to the cell, or comprising the administration of an nm23H1 or nm23H2 polypeptide of disclosed sequence to the cell in an organism, and since determination of these factors is highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO

DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JZ
9-28-04

J. Zara
TC 1600